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Award Number: W81XWH-11-2-0107

**TITLE:** Assessment of Chiropractic Treatment for Low Back Pain, Military Readiness and Smoking Cessation in Military Active Duty Personnel

**PRINCIPAL INVESTIGATOR:** Ian Coulter

**CONTRACTING ORGANIZATION:** RAND Corporation

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14. ABSTRACT  This study is comprised of three trials, referred to as the Assessment of Chiropractic Treatment (ACT). The most significant work during the last reporting period has occurred in the first study, referred to as ACT 1 which is a randomized controlled trial of chiropractic for low back pain with a nested smoking cessation component in active duty military personnel. During this reporting period ACT 1 met 46% of its recruiting target. For the second study, referred to as ACT 2 which is a randomized controlled trial of response and reaction times in Special Operations Forces, the pilot feasibility testing in civilian population has been completed and a study redesign has passed through IRB approvals after redesign to include a waitlist control group. For the third study, referred to as ACT 3 which is a randomized controlled trial of strength, balance, and re-injury comparing standard care with standard care plus chiropractic treatment, final IRB approvals have been received and this study is going into pilot testing phase after a redesign which removed the sham treatment.					
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## **INTRODUCTION:**

This annual report provides updates for the reporting period February 15, 2013 through February 14, 2014 on the study "Assessment of Chiropractic Treatment for Low Back Pain, Military Readiness and Smoking Cessation" (Grant Number W81XWH-11-2-0107). This program consists of three trials taking place at five military sites under the study. These trials have staggered start dates at multiple sites. Trial A is a randomized controlled trial of low back pain with nested smoking cessation for active duty personnel at Walter Reed National Military Medical Center in Bethesda, MD; Naval Hospital Pensacola, FL; Naval Medical Center San Diego, CA) which was the first study to be initiated. This study is followed by consecutively run Trials B and C. Trial B was previously a cohort of reflexes and reaction times, now it is a randomized controlled trial of response and reactions times in Special Operations Forces at Blanchfield Army Community Hospital, Fort Campbell, KY. Trial C is a randomized controlled trial of strength, balance, and Low Back Pain Recurrence for active duty at Madigan Army Medical Center, Joint Base Lewis-McChord, WA.

## **BODY:**

### ***Clinical Trial A (ACT 1) Summary***

Assessment of Chiropractic Trials Study A (called "ACT 1") is a multi-site randomized controlled trial (RCT) for low back pain with nested smoking cessation study at sites: Walter Reed National Military Medical Center in Bethesda, MD; Naval Hospital Pensacola, FL; Naval Medical Center San Diego, CA. The aim of ACT 1 is to conduct a multi-site, randomized controlled trial to test whether the combination of chiropractic treatment plus standard medical care is superior to standard medical care alone for relief of pain and the improvement in function in active duty military personnel (ages 18-50) with acute, sub-acute and/or chronic, non-surgical low back pain. During this reporting period, 46% of the recruitment target has been met: a total of 353 participants have been recruited with 154 at Naval Medical Center San Diego (NMCS), 132 at Naval Hospital Pensacola (NHP), and 67 at Walter Reed National Military Medical Center in Bethesda (WRNMMC), MD.

Recruitment strategies at each site have evolved greatly during this reporting period highlighting the marked variability in population at each military site (see tables in Task 8). Given these differences, each site has adapted a recruitment plan that fits the infrastructure of the base and accomplishes the goals of the study at the same time. The ability to adapt the recruitment plan to each site and work with military command has proven very successful. We are on track to recruit 8-10 participants per month for the next reporting period.

During this reporting period, we have developed an internal quality assurance program where the Lead Project Manager (PM) or designated staff member reviews the regulatory documents as well as a percentage of study data collected at each site. This process is currently being finalized. In summary, the lead PM or designee visits each site on a quarterly basis to review the site regulatory binder, all informed consent documents, as well as data collection forms compared to what is entered in the web-based repository for study data. This process has improved the quality and integrity of our study data, improved the process for data collection and entry, as well as provided another level of oversight that was greatly needed especially as the rate of study accrual continued to rise.

Another effort implemented during this period to assist in the management of the regulatory procedures across sites was the development of both an Internal Review Board (IRB) reporting spreadsheet to track all IRB submissions as well as timelines for continuing reviews for the 5 IRBs involved in this study (3 military, RAND IRB, Palmer College IRB). Additionally, a schematic for reporting adverse events as well as protocol deviations and unanticipated events was also

developed to ensure proper reporting of study events to respective IRBs. The schematic lists the reporting requirements for each IRB with the respective timelines for doing so. This process has greatly improved the ability to manage these events across multiple IRBs and has also led to improvement in the quality surrounding the process for documentation of these events should they occur.

During this reporting period, there was a change in site Principal Investigator at the Walter Reed National Military Medical Center. LCDR Robert Rosenbaum retired and MAJ Keith Myers resumed the position of site PI (June 2013). In addition, the WRNMMC medical monitor LCDR Christopher Neal was transferred and therefore, Dr. Alison Pruziner assumed this role effective February, 4 2014.

Further, pilot data that was used to design and refine the protocol for ACT 1 was published in *Spine*. It is a randomized controlled trial to assess changes in pain levels and physical functioning in response to standard medical care (SMC) *versus* SMC plus chiropractic manipulative therapy (CMT) for the treatment of low back pain (LBP) among 18 to 35-year-old active-duty military personnel. It is attached in Appendix A.

Additional personnel changes during this reporting period:

- Bridget Kane transitioned from site Project Manager at WRNMMC to Lead Clinical Project Manager, replacing Dr. Katie Pohlman, for the ACT studies on May 13, 2013.
- Diane Pizzano assumed the site Project Manager position at WRNMMC on September 16, 2013.
- Erin Cesario assumed site Project Manager Position, replacing Amy Engel, at NMCSO on January 6, 2013.

Task 1: Submit quarterly technical progress reports to project officers

- In compliance with reporting requirements, quarterly reports were submitted in this reporting period on the following dates: May 15, 2013, August 16, 2013, and November 15, 2013.

Task 2: Annual reports have gone to U.S. Army Medical Research and Materiel Command

- In compliance with reporting requirements, annual reports were submitted on March 14, 2012 and March 15, 2013.

Task 3: Finalized protocol and sites

- No changes in sites since end of last reporting period
- Minor changes in protocol as detailed in Task 6.
- Initiated recruitment at Walter Reed National Military Medical Center (March, 18, 2013)

Task 4: Convened advisory panel for review of all study matters

- Addressed remaining issues with advisory panel last reporting period when convened panel on May 1, 2012.

Task 5: Prepared data collection systems

- Loaded all coded outcomes instruments onto data management system, by visit/data collection point

- Identified data entry/data verification personnel
- Developed web reports to track and manage participant completion of outcome assessments at each time point (week, 2, week 4, week 6, and month 3)
- Developed web report to monitor participant enrollment and status at each time point across all 3 sites
- Developed module to collect data from Computer Assisted Telephone Interview (CATI)
- Designed module to record chiropractic visit data

#### Task 6: IRB approval processes and other regulatory requirements

- In terms of IRB processes, the amendments to protocol reflect minor changes in procedures such as broadening recruitment strategies, changes to forms and consent language based on looping through three military IRB reviews, RAND and Palmer College human subjects review committees.
- There were a series of IRB approvals in sequence that we worked through, including local military scientific and IRB reviews, RAND, Palmer College, and second level Human Research Protection Office (HRPO) approvals. As follows:
- There was an amendment to the Cooperative Research and Development Agreement (CRADA) executed on August 14, 2013.

#### Walter Reed National Military Medical Center in Bethesda, MD

- Initial submission October 18, 2012
- Amendment 01 February 4, 2013
- Amendment 02 May 21, 2013
- Amendment 03 September 24, 2013
- Amendment 04 February 4, 2014

#### Naval Hospital Pensacola, FL (IRB of record: Naval Medical Center Portsmouth)

*\*\* Approval date indicates both Portsmouth approval as well as Commanding Officer of Naval Hospital Pensacola approval*

- Initial submission August 1, 2012
- Amendment 01 September, 17, 2012
- Amendment 02 January 31, 2013
- Amendment 03 April 12, 2013
- Amendment 04 September 6, 2013
- Data Sharing Agreement October 7, 2013, January 22, 2014

#### Naval Medical Center San Diego, CA

- Initial submission February 22, 2012
- Amendment 01 August 6, 2012
- Amendment 02 March 13, 2013
- Amendment 03 November 1, 2013
- Amendment 04 January 22, 2014
- Data Sharing Agreement September 23, 2013, February 18, 2014

RAND Corporation: ACT 1 gained initial approval on January 20, 2011 with amendments to procedures approved on the following dates:

- Amendment 01 July 28, 2011

- Amendment 02 August 9, 2011
- Amendment 03 January 31, 2012
- Amendment 04 April 12, 2012
- Amendment 05 May 15, 2012
- Amendment 06 September 16, 2012
- Amendment 07 January 2, 2012
- Amendment 08 August 21, 2013
- Amendment 09 November 7, 2013
- Event Report 01 March 4, 2013 on a patient with gall bladder surgery that was deemed not connected to study
- Event Report August 13, 2013 on an allocation algorithm error which was corrected.

Palmer College of Chiropractic:

- Initial Submission January 18, 2011
- Amendment 01 March 9, 2011
- Amendment 02 March 16, 2011
- Amendment 03 June 6, 2011
- Amendment 04 December 7, 2011
- Amendment 05 February 7, 2012
- Amendment 06 March 19, 2012
- Amendment 07 May 4, 2012
- Amendment 08 May 11, 2012
- Amendment 09 July 26, 2012
- Amendment 10 January 11, 2013
- Amendment 11 November 15, 2013
- System Security Verification September 10, 2013

Second Level Review at USAMRMC:

- The ACT 1 protocol was reviewed by the U.S. Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO) and found to comply with applicable DOD, U.S. Army and USAMRMC human subjects protection requirements on February 9, 2012.

Task 7: Hired and trained study coordinators for each site

- Developed standard employment contract
- Train study coordinators in standardized methods, including data entry and management
  - *WRNMMC, Bethesda, MD – March 18, 2013* – Lead Project Manager (PM), Dr. Katie Pohlman met with WRNMMC site PM, Bridget Kane, and Ms. Kane walked through all of the recruitment efforts that had been established.
  - *WRNMMC, Bethesda, MD – September 16-18, 2013* - Bridget Kane, Lead PM, went to WRNMMC on September 16-18, 2013 to train new site PM Diane Pizzano. Training started in Bethesda, MD on site for one week and continued in Davenport, IA at the Palmer Center for Chiropractic Research for week two. Ms. Pizzano is fully operational on-site at WRNMMC. During this visit, Ms. Kane was

able to meet with MAJ Keith P. Myers, Site PI as well as study doctors of chiropractic, Drs. William Morgan and Kearney. All were eager to renew study recruitment efforts.

- *NMCSD, San Diego, CA – January 6-10, 2014* –Erin Cesario assumed the role of site Project Manager at NMCSD on January 6, 2014. Her first phase of training took place at the Palmer Center for Chiropractic Research January 6, 2014 – January 10, 2014. She received additional on-site training at WRNMMC, Bethesda, MD on January 27, 2014 through January 31, 2014 by WRNMMC site Project Manager, Diane Pizzano. Ms. Cesario began recruitment at NMCSD the week of February 3, 2014.
- All study coordinators trained and certified for site-specific CITI
  - All human subject's protections certifications current through reporting period
- Obtained ID badges and security approvals for all on-site study personnel
  - U.S. government security clearances and Common Access Card (CAC) obtained for all ACT 1 staff during this reporting period
- Conducted administrative site visits to ensure all systems are in place and fully functional. Site visits for ACT 1 during this reporting period include:
  - *NMCSD, San Diego, CA – May 02, 2013* - Dr. Christine Goertz (PI) met with site PM, Amy Engel. They celebrated the success of this site meeting 25% of its recruitment goal. They also met with the Commanding Officer of the North Island branch medical center to discuss continued support to have the eligibility exam completed with the decrease in the number of independent duty corpsman (IDC). The Commanding Officer assured Dr. Goertz and Ms. Engel that support remain in place.
  - *NMCSD, San Diego, CA – June 16, 2013* – Dr. Christine Goertz (PI) met with CDR Christopher Chisholm, Officer in Charge of the Naval Branch Health clinic, and Dr. David Ward, study Doctor of Chiropractic. Dr. Goertz thanked CDR Chisholm for his support in allowing the Independent Duty Corpsmen (IDCs) to conduct study physical exams. She explained the positive impact this has made on study flow and recruitment at the site. CDR Chisholm reaffirmed his support for our study. Dr. Goertz also discussed study timelines and recruitment status with Dr. Ward.
  - *WRNMMC, Bethesda, MD - June 24, 2013* – Dr. Christine Goertz (PI) came to the WRNMMC on June 24, 2013 and met with Major Keith Myers. MAJ Myers has assumed the site PI position due to LCDR Robert Rosenbaum's retirement from the U.S. Navy. Dr. Goertz discussed role and responsibilities of being a site PI with MAJ Myers as well as the goals and status of the ACT 1 study. During this visit, Dr. Goertz also met with Dr. Bill Morgan, study Doctor of Chiropractic.
  - *Naval Hospital Pensacola, Florida – August 22, 2013* – Dr. Christine Goertz (PI) conducted a site visit on August 22, 2013. During this visit, Dr. Goertz met with CDR Joseph F. Penta (site PI), Dr. Greg Lillie, study Doctor of Chiropractor, and Wendy Freiburger, Site PM. Study time lines and recruitment status were discussed. Additionally, Dr. Goertz met the new OIC of the Naval Air Technical Training Center, Naval Health Branch Clinic (NHBC), LCDR Adrian Gaskin. Dr. Goertz discussed the ACT 1 study purpose and status with the OIC; the OIC is in support of the ACT 1 study.
  - *NMCSD, San Diego, CA - November 19- November 22, 2013* – Bridget Kane, Lead Clinical Project Manager, met with site Project Manager, Amy Engel to discuss transition plan due to Ms. Engel's resignation (effective December 3, 2013). All study documentation was reviewed during this visit. During this visit, Ms. Kane also met with Ms. Rhonda Allen in the Clinical Investigations Department at NMCSD to discuss personnel changes within the study and ascertain procedures for processing Ms. Engel's resignation as well as the procedures hiring and processing new research staff. Ms. Kane interviewed Erin Cesario, candidate for site Project Manager at



NMCS D during this visit. Finally, Ms. Kane met with CAPT Rosenthal (site PI), CDR Chisholm (OIC of North Island Naval Branch Health Clinic), and Dr. David Ward, study Doctor of Chiropractor to apprise the team of the transition plan for site Project Manager.

**Task 8: Study recruitment and data collection per site for reporting period:**

During this reporting period, 46% of the recruitment target has been met: a total of 353 participants have been recruited with 154 at Naval Medical Center San Diego, 132 at Naval Hospital Pensacola, and 67 at Walter Reed National Military Medical Center in Bethesda, MD. We had hoped to have higher recruitment at Walter Reed National Military Medical Center but it has fallen slightly due to personnel changes in the summer. The Project Manager has been replaced and we expect recruitment to increase in the next reporting period. Table 1 below displays the recruitment, accrual and retention data. Participant characteristics and recruitment graphs are displayed below for each site.

**Table 1: Recruitment, Accrual and Retention**

As of Feb 14 2014	NMCS D: San Diego	NHP: Pensacola	WRNMMC: Bethesda	Total
<b>Baseline</b>	<b>178</b>	<b>142</b>	<b>75</b>	<b>395</b>
# excluded	21	10	0	31
# chose not to participate	2	0	7	9
<b>Allocated</b>	<b>154</b>	<b>132</b>	<b>67</b>	<b>353</b>
<b>Week 2 Assessment</b>	<b>149</b>	<b>130</b>	<b>62</b>	<b>341</b>
# completed	133	95	56	284
# missed outcomes	16	33	4	53
% missed outcomes	11%	24%	3%	14%
# withdrawn	0	2	2	4
<b>Week 4 Assessment</b>	<b>149</b>	<b>125</b>	<b>59</b>	<b>333</b>
# completed	125	85	55	265
# missed outcomes	23	40	4	67
% missed outcomes	15%	32%	7%	20%
# withdrawn	1	0	0	1
<b>Week 6 Assessment</b>	<b>148</b>	<b>125</b>	<b>54</b>	<b>327</b>
# completed	141	103	54	298
# missed outcomes	6	19	0	25
% missed outcomes	3%	13%	0%	6%
# withdrawn	1	3	0	4
<b>Month 3 Assessment</b>	<b>145</b>	<b>116</b>	<b>37</b>	<b>298</b>
# completed	127	93	36	256
# missed outcomes	17	21	1	39
% missed outcomes	11%	16%	3%	12%
# withdrawn	1	2	0	3

## Data for Naval Hospital Pensacola, FL

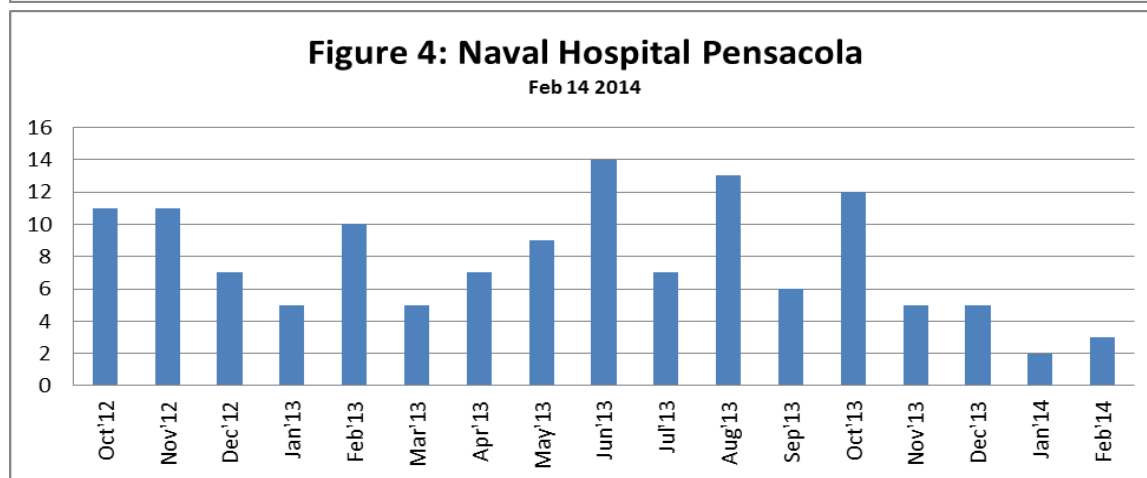
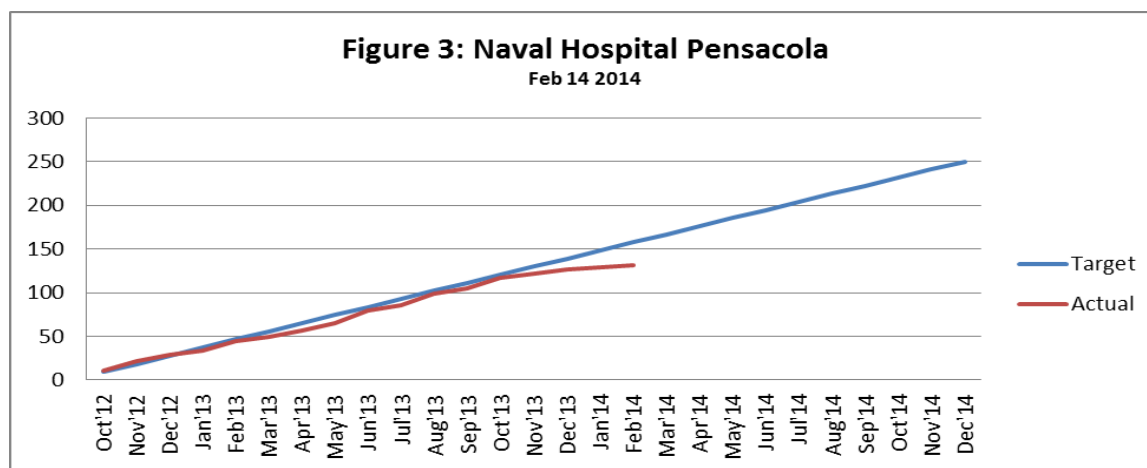
**Table 3: Demographics for Annual Report of Project DoD ACT1\***

As of Feb 14 2014

Questions	Values	Treatment 1 (n=66)		Treatment 2 (n=66)		Total (n=132)	
		n	%	n	%	n	%
<b>Ethnic</b>	Hispanic or Latino	14	21	9	14	23	17
	Not Hispanic or Latino	50	76	56	85	106	80
	Unspecified	2	3	1	1.52	3	2
<b>Sex</b>	Female	9	14	9	14	18	14
	Male	57	86	57	86	114	86
<b>Race</b>	American Indian or Alaska Native	0	0	0	0	0	0
	Asian	2	3	1	2	3	2
	Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0
	Black or African American	10	15	7	11	17	13
	White	51	77	55	83	106	80
	Multi-racial	1	2	0	0	1	1
	Unspecified	2	3	3	5	5	4
<b>Age</b>	Mean SD	24.7	6.9	24.6	6.7	24.6	6.8
	Median	22.0		22.5		22.0	
	n	66		66		132	

\* this table is for **Naval Hospital in Pensacola**

percentages may not add up to 100 due to rounding



## Data for Naval Medical Center San Diego, CA

**Table 4: Demographics for Annual Report of Project DoD ACT1\***

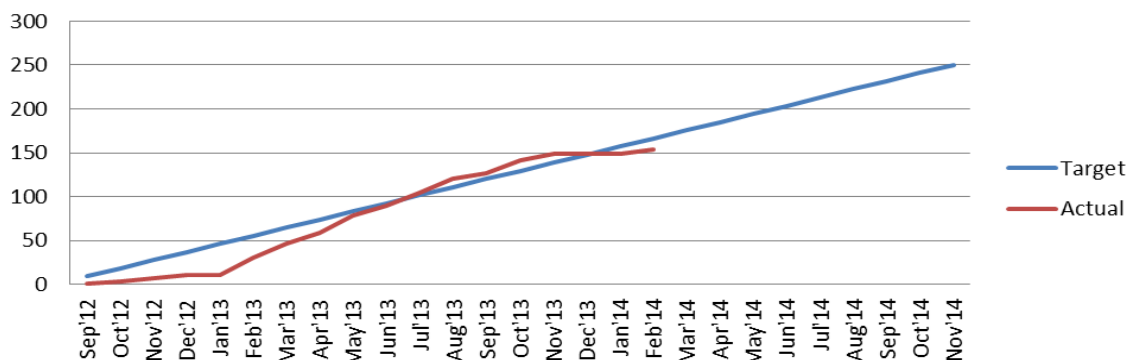
As of Feb 14 2014

Questions	Values	Treatment 1 (n=77)		Treatment 2 (n=77)		Total (n=154)	
		n	%	n	%	n	%
<b>Ethnic</b>	Hispanic or Latino	14	18	15	19	29	19
	Not Hispanic or Latino	62	81	59	77	121	79
	Unspecified	1	1	3	4	4	3
<b>Sex</b>	Female	14	18	13	17	27	18
	Male	63	82	64	83	127	82
<b>Race</b>	American Indian or Alaska Native	1	1	0	0	1	1
	Asian	8	10	5	6	13	8
	Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0
	Black or African American	9	12	11	14	20	13
	White	59	77	61	79	120	78
	Multi-racial	0	0	0	0	0	0
	Unspecified	0	0	0	0	0	0
<b>Age</b>	Mean SD	32.4	6.9	32.8	7.5	32.6	7.2
	Median	32.0		33.0		32.0	
	n	77		77		154	

\* this table is for **Naval Medical Center in San Diego**  
percentages may not add up to 100 due to rounding

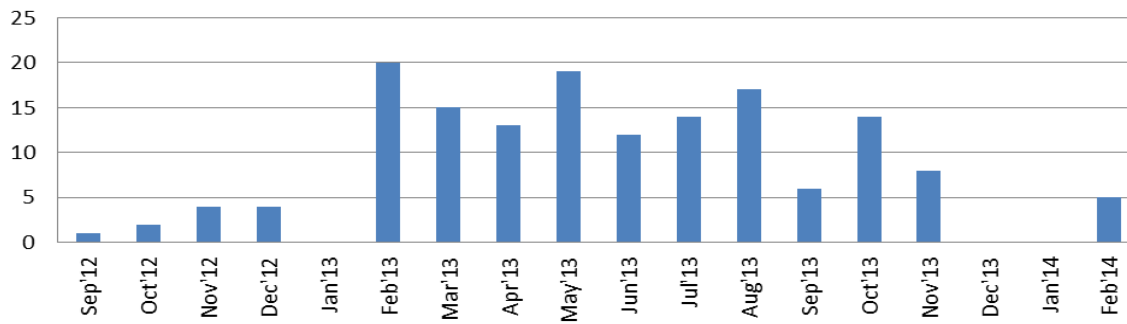
**Figure 5: Naval Medical Center San Diego**

Feb 14 2014



**Figure 6: Naval Medical Center San Diego**

Feb 14 2014



Data for Walter Reed National Military Medical Center in Bethesda, MD

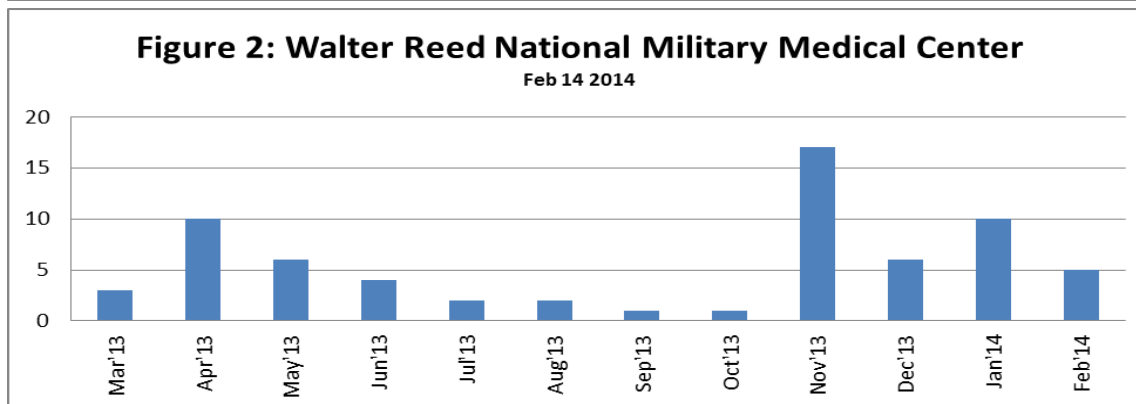
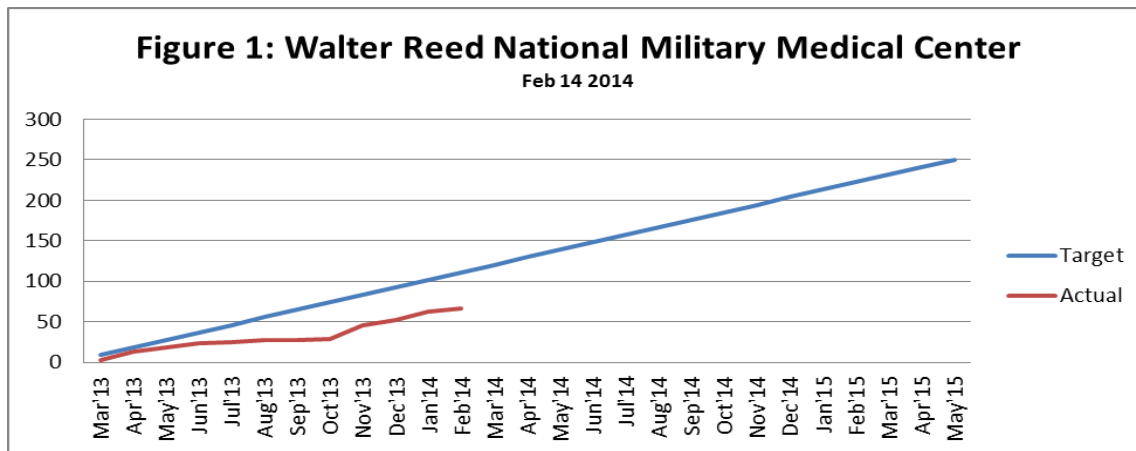
Table 2: Demographics for Annual Report of Project DoD ACT1\*

As of Feb 14 2014

Questions	Values	Treatment 1 (n=34)		Treatment 2 (n=33)		Total (n=67)	
		n	%	n	%	n	%
Ethnic	Hispanic or Latino	5	15	1	3	6	9
	Not Hispanic or Latino	27	79	31	94	58	87
	Unspecified	2	6	1	3	3	4
Sex	Female	11	32	10	30	21	31
	Male	23	68	23	70	46	69
Race	American Indian or Alaska Native	0	0	0	0	0	0
	Asian	1	3	1	3	2	3
	Native Hawaiian or Other Pacific Islander	1	3	1	3	2	3
	Black or African American	11	32	10	30	21	31
	White	17	50	19	58	36	54
	Multi-racial	1	3	0	0	1	1
	Unspecified	3	9	2	6	5	7
Age	Mean SD	35.9	7.6	35.7	7.7	35.8	7.6
	Median	36.0		36.0		36.0	
	n	34		33		67	

\* this table is for **Walter Reed National Military Medical Center in Bethesda**

percentages may not add up to 100 due to rounding



Task 9: Quality assurance site visits conducted during this period included:

- Walter Reed National Military Medical Center in Bethesda, MD (Not applicable during this period)
- Naval Hospital Pensacola, FL
  - October 28-29, 2013 (ACT 1) - Bridget Kane, Lead Clinical Project Manager, and Gwen Abdulhafid, ACT 2 site Project Manager, conducted an internal quality assurance review. Study informed consent documents, physician exam forms, and chiropractic data collection forms were reviewed for error. This process will be repeated on a quarterly basis. During this visit, Bridget Kane also met with Site PI, CDR Joseph Penta and study doctor of chiropractic, Dr. Gregory Lillie. Recruitment status was reviewed as well as the results of the quality assurance review.
- Naval Medical Center San Diego, CA
  - *July 29, 2013 – August 1, 2013* - Gwen Abdulhafid, ACT 2 site Project Manager, conducted an internal quality assurance review. Study informed consent documents, physician exam forms, and chiropractic data collection forms were reviewed for error.
  - *August 26-27, 2013* - Bridget Kane, Lead PM, went to NMCS D to review findings from quality assurance review conducted in July of 2013. Ms. Kane also reviewed Informed Consent Documents (ICDs), study exam forms, chiropractic data collection forms, and all regulatory documentation. Ms. Kane also met with Dr. David Ward, site chiropractor, and discussed study status as well as findings from the quality assurance review.

Task 10: Write methodology manuscript for submission (Not applicable during this reporting period)

- An initial draft of the ACT I methodology manuscript has been completed. We anticipate submitting it for publication during the next reporting period.

Task 11: Submit annual continuing review documents for IRB. The following IRB continuing reviews have been processed on these dates:

- Walter Reed National Military Medical Center in Bethesda, MD received continuing review approval on November 21, 2013.
- Naval Hospital Pensacola, FL received continuing review approvals on December 13, 2012 and January 21, 2014.
- Naval Medical Center San Diego, CA received continuing review approvals on January 9, 2013 and December 23, 2013.
- RAND Corporation gained continuing review approvals on January 13, 2012, December 18, 2012, and November 20, 2013.
- Palmer College received continuing review approvals on January 19, 2012, January 18, 2013, and February 3, 2014.
- USAMRMC: The ACT 1 protocol was reviewed by the U.S. Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO) and found to comply with applicable DOD, U.S. Army and USAMRMC human subjects protection requirements initially on February 9, 2012, with continuing review on January 28, 2013 and January 14, 2013.

Task 12: Convene advisory board at yearly intervals and as needed (Annually) RAND

- Convened advisory panel on May 1, 2012 and another advisory meeting is in planning stages during the end of the current reporting period to meet in March 2014.

Task 13: Close study recruitment (Not applicable during this reporting period)

Task 14: Analyze data (Not applicable during this reporting period)

Task 15: Write final study reports and manuscript (Not applicable during this reporting period)

Task 16: Convene publications committee at Month 18 and quarterly thereafter (Not applicable during this reporting period)

### ***Clinical Trial A (ACT 1) Summary of Tobacco Cessation Trial***

The aim of this nested trial within Trial A is to measure changes in smoking and tobacco behavior between two treatment groups, in response to a tobacco cessation program delivered in the chiropractic arm of the study, in a nested study design. Investigation of a smoking cessation program delivered by Doctors of Chiropractic will be imbedded in the low back pain trial. Those who wish to participate in the low back pain study but not the smoking cessation program will be allowed into the study. During this reporting period, a newsletter was developed that will be delivered electronically every 6 months for the purpose of re-training the chiropractors on content related to conducting the tobacco cessation nested study.

Task 1: Finalized manual and other program materials

- Adapt and revise program for military population and tobacco users
- Adapt patient materials to military population(s)

Task 2: Train chiropractors to deliver program in standardized fashion (Months 6-12) Palmer

- Pilot tested delivery and assess standardization
- The study doctors of chiropractic were re-trained per study protocol on June, 17, 2013 and on February 3, 2014 via an electronic newsletter.

Task 3: Finalized outcome parameters for tobacco cessation, loaded onto system

Task 4: Data Collection underway as follows:

<b>Table 5: Tobacco Enrollment Report</b>				
	<u><b>Tobacco User</b></u>	<u><b>Consented</b></u>	<u><b>Enrolled</b></u>	<u><b>Withdrawn</b></u>
Walter Reed National Military Medical Center	6	4	1	1
Naval Hospital Pensacola	29	22	8	2
Naval Medical Center San Diego	40	26	10	1

Task 5: Data Analysis (Not applicable during this reporting period)

### ***Clinical Trial B (ACT 2) Summary***

The specific aim for ACT 2 was previously to assess military readiness by evaluating pre-post differences in reflexes and reaction times following chiropractic treatment in members of Special Operation Forces at Blanchfield Army Community Hospital, Fort Campbell, KY. Based on feedback from the scientific review committee (received July 12, 2013) at Dwight D. Eisenhower (IRB of record for Fort Campbell), the study design has been altered to a randomized controlled trial of chiropractic treatment versus waitlist control group and the population has been better described to include only Special Operations Forces who are qualified for operations, meaning that support staff are excluded. The Dwight D. Eisenhower Army Medical Center IRB contingently approved the ACT 2 study protocol on December 12, 2013. We are awaiting final approval from USAMRMC Clinical Investigations Review Office (CIRO). Hiring and training of the ACT 2 site PM will commence during the next reporting period.

The ACT 2 pilot study was completed on May 8, 2014. The results of this study supported the addition of an initial assessment visit as well as the addition of a control group to reduce and account for potential learning effects associated with repeated measurements of the different reaction time tests.

Also during this reporting period, the Clinical Trial Coordinating Center (CTCC) developed the web application to support the conduct and data collection of the ACT 2 study.

#### **Task 1: Make final selection of Special Forces site(s)**

- Blanchfield Army Community Hospital, Fort Campbell, KY was identified as the single site for ACT 2. During the last reporting period it was noted that we no longer had support to conduct a study in Special Operations Forces at Joint Base Lewis-McChord. On July 8, 2013 leadership at Naval Medical Center San Diego withdrew support to work with Special Operations Forces. However, with the new study design and fewer sample size needed to power statistical analyses, the single site at Fort Campbell will be sufficient for this study. The Department of Navy CRADA was revised and executed on August 14, 2013 to reflect this change.

#### **Task 2: Finalized metrics for response and reaction times**

- The protocols for the 5 different reaction time tests as well as the data collection forms were refined based on the findings of the pilot study. Metrics associated with electromyographic (EMG) measurements (not included in the original proposal) were dropped due to multiple problematic issues associated both with the data collection and the analysis of the data.

#### **Task 3: IRB approval process**

- Worked through sequences of IRB approvals, including local military scientific and IRB reviews, RAND, Palmer College, and second level Human Research Protection Office (HRPO) approvals. As follows:
- Dwight D. Eisenhower Army Medical Center (Fort Campbell's IRB of record)
  - Initial submission December 12, 2013 (contingent approval)
- RAND Corporation
  - Initial submission December 6, 2012
  - Pilot approval May 10, 2012
  - Continuing review May 31, 2013
  - Amendment 01 August 21, 2013
  - Amendment 02 February 14, 2014 (re-design approved)

- Palmer College (pilot)
  - Initial submission May 22, 2012
  - Amendment 01 January 10, 2013
  - Continuing Review/Close-out May 21, 2013
- Palmer College (Military study)
  - Initial submission February 2, 2012
  - Amendment 01 May 1, 2012
  - Amendment 02 June 14, 2012
  - Amendment 03 January 9, 2013
  - Continuing Review 01 January 23, 2013
  - Continuing Review 02 January 24, 2013
- USAMRMC: The ACT 2 protocol was reviewed by our officer at the Clinical Investigation Regulatory Office, Office of Research Protections, U.S. Army Medical Research and Materiel Command and she was awaiting approval authority at the close of this reporting period. We anticipate approval without incident shortly.

#### Task 4: Study recruitment and data collection

- Pilot study recruitment and data collection efforts are as follows:
- Recruitment for the ACT 2 pilot study commenced on August 14, 2012 and was completed on May 1, 2013 for a total of 17 enrolled participants. Data collection was completed on May 8, 2014.
- The main study involving Special Operations Forces has not moved into recruitment phase by the end of this reporting period.

#### Task 5: Quality assurance site visits

- Staff training
  - *Site Project Manager* – Gwen Abdulhafid was hired on April 12, 2013 to manage the ACT 2 study at Ft. Campbell, KY. She was extensively trained at the Palmer Center for Chiropractic Research from May 6, 2013 – May 10, 2013, at WRNMMC, Bethesda from May 20, 2013 – May 22, 2013; at Ft. Campbell, KY from June 4, 2013 – June 5, 2013; and at Naval Hospital Pensacola from June 6, 2013 – June 7, 2013.
- Study logistics
  - *June 03/04, 2013* - Gwen Abdulhafid (Site PM), Bridget Kane (Lead PM), Jim DeVocht (Study Investigator), Dean Smith (Study Consultant), Katie Pohlman (Study Consultant) conducted a site visit on June 3, 2013 and June 4, 2013. During this visit, the biomechanical assessment equipment was set up on site and final signatures were obtained for site IRB review. Project investigators discussed logistics of recruitment and study flow within the provided area. The biomechanical assessments were tested and the full site study team was trained on the use of this equipment.
  - *September 24, 2013* - ACT 2 Palmer College Project Leader, Dr. Jim DeVocht, and site Project Manager, Gwen Abdulhafid, conducted a site visit to Ft. Campbell to make some revisions on the software for data collection. During this visit, Dr. DeVocht and Ms. Abdulhafid were also able to meet with Dr. Tom Jones, Site PI and study doctor of chiropractic, Dr. Sean Suttles, physical therapist, and Dr. Lisa Giarrizzo, Chief of Surgery at Blanchfield Army Community Hospital and newly appointed study medical monitor.



Essential regulatory documents were collected and study start-up timelines were reviewed.

- *October 21, 2013* - Dr. Christine Goertz, PI, and Gwen Abdulhafid, site Project Manager, met with Dr. Tom Jones, site PI, and Dr. Sean Suttles, research study staff, at Ft. Campbell on October 21, 2013. Study start-up time lines were reviewed with staff as well as the status of current IRB submission.

Task 6: Analyze pre-post data (Not applicable during this reporting period)

### ***Clinical Trial C (ACT 3) Summary***

The original aim outlined in the grant proposal for ACT 3 was to assess military readiness by evaluating differences in strength, balance, and injury prevention between CMT and sham manipulation in members of the Armed Forces eligible for combat deployment. Since the submission of the proposal, findings from one of our recently completed studies evaluating postural sway (balance) following spinal manipulation compared to a sham, as well as a study published by another investigator evaluating the number of visits for spinal manipulation have prompted us to propose a new design. The major finding was that the two balance tests used in the study did not demonstrate any between-group difference when compared to the sham group at the two week time point. Secondary clinical outcomes including NRS pain and RMDQ showed a small but statistically significant decrease at the two week point. Further, data suggest that 12 chiropractic visits may be optimal for maximizing treatment effects.

Further, conversations with the new officer in charge of the chiropractic department at Joint Base Lewis-McChord has expressed concern regarding the use of sham manipulation in volunteers suffering from low back pain. Based on his concerns and findings from these two studies, we changed the ACT 3 study design to a randomized controlled trial evaluating the effects of six weeks of standard medical care versus standard medical care plus chiropractic care on strength, balance, and injury prevention (recurrence of low back pain) in members of the Armed Forces eligible for combat deployment. This design would offer a more pragmatic approach, and ensures that all participants will receive treatment for their low back pain. Further, results may more generalizable and thus valuable to military populations.

Task 1: Established metrics for strength, balance, re-injury

- Ensured standardized training of research personnel in taking and recording these measurements
- Established inter-rater reliability
- Identified and secured additional equipment necessary to take measurements

Task 2: IRB approval process

- Worked through sequences of IRB approvals, including local military scientific and IRB reviews, RAND, Palmer College, and second level Human Research Protection Office (HRPO) approvals. As follows:
- Madigan Army Medical Center IRB: (Not applicable during this reporting period)
- RAND Corporation:
  - Initial approval                      October 1, 2013
  - Amendment 01                      November 15, 2013
  - Amendment 02                      Pending for redesign the redesign replacing standard care for sham in the control group.
- Palmer College
  - Main study
    - Initial approval                      August 17, 2012

- Amendment January 10, 2013
  - Continuing review approval August 19, 2013
- Pilot study
  - Initial submission January 11, 2013
  - Amendment 01 May 10, 2013
  - Amendment 02 June 24, 2013
  - Amendment 03 July 10, 2013
  - Amendment 04 October 7, 2013
  - Continuing review 01 January 16, 2014
- USAMRMC: The ACT 3 protocol has not been reviewed by our officer at the Clinical Investigation Regulatory Office, Office of Research Protections, U.S. Army Medical Research and Materiel Command. We anticipate submission to second level review after local military, RAND, and Palmer College IRB approvals are garnered.

Task 3: Prepared data collection system: Coded all data parameters and load onto data collection system

Task 4: Consulted advisory panel on validity/relevance of selected outcomes measures: Addressed issues with advisory panel last reporting period during convened panel on May 1, 2012.

Task 5: Recruit and enroll subjects and collect data (Not applicable during this reporting period)

Task 6: Quality assurance site visits

- Study logistics
  - *August 29, 2013* - Dr. Rob Vining (Senior Research Clinician at Palmer Center for Chiropractic Research and Associate Investigator), Dr. Ram Gudavalli (Associate Investigator, Palmer Center for Chiropractic Research), Dr. Katherine Pohlman, Study consultant, and Bridget Kane, Lead PM conducted a pre-study visit for ACT 3 on August 29, 2013 at Madigan Army Medical Center. Study logistics were discussed with MAJ Daniel Rhon, Site PI and Dr. Todd O'Mealy, site Doctor of Chiropractic.

Task 7: Analyze data and write final study reports (Not applicable during this reporting period)

## **KEY RESEARCH ACCOMPLISHMENTS ACROSS ALL STUDIES:**

Key research accomplishments are as follows:

ACT 1:

- Recruitment has reached 46% for ACT 1 trial for low back pain and tobacco cessation.

ACT 2:

- Initial IRB approvals gained at military site, RAND, and Palmer College
- Revised protocol with redesign, gained provisional approval for redesign at Ft. Campbell
- Hired new Project Manager at Ft. Campbell, KY

ACT 3:

- Revised protocol with redesign based on significant new data and site leadership input at Joint Base Lewis-McChord.
- Uploaded all components to military IRBnet and awaiting command signature to process.

**REPORTABLE OUTCOMES ACROSS ALL STUDIES:**

Not applicable during this reporting period.

**CONCLUSIONS:**

The significance of this research is high. Low back pain is a prevalent public health problem in both the military and civilian populations. Currently a clear “gold standard” medical treatment for low back pain does not exist and studies show that evidence-based guidelines are rarely used in general practice. Thus, there is a need to consider innovative treatment options for chronic diseases such as low back pain. Our preliminary data suggested that chiropractic treatment in addition to standard medical care may be superior to standard medical care alone in active duty service members. In addition, doctors of chiropractic are well positioned to provide information to support smoking cessation. The results from this set of trials provide critical information regarding the health and mission-support benefits of chiropractic health care delivery for active duty service members in the military.

**REFERENCES:** No references.

**APPENDICES:**

Appendix A. SPINE Article

**SUPPORTING DATA:**

Not applicable during this reporting period.

## RANDOMIZED TRIAL

# Adding Chiropractic Manipulative Therapy to Standard Medical Care for Patients With Acute Low Back Pain

## Results of a Pragmatic Randomized Comparative Effectiveness Study

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**Study Design.** Randomized controlled trial.

**Objective.** To assess changes in pain levels and physical functioning in response to standard medical care (SMC) versus SMC plus chiropractic manipulative therapy (CMT) for the treatment of low back pain (LBP) among 18 to 35-year-old active-duty military personnel.

**Summary of Background Data.** LBP is common, costly, and a significant cause of long-term sick leave and work loss. Many different interventions are available, but there exists no consensus on the best approach. One intervention often used is manipulative therapy. Current evidence from randomized controlled trials demonstrates that manipulative therapy may be as effective as other conservative treatments of LBP, but its appropriate role in the healthcare delivery system has not been established.

**Methods.** Prospective, 2-arm randomized controlled trial pilot study comparing SMC plus CMT with only SMC. The primary outcome measures were changes in back-related pain on the numerical rating scale and physical functioning at 4 weeks on the Roland-Morris Disability Questionnaire and back pain functional scale (BPFS).

**Results.** Mean Roland-Morris Disability Questionnaire scores decreased in both groups during the course of the study, but adjusted mean scores were significantly better in the SMC plus

CMT group than in the SMC group at both week 2 ( $P < 0.001$ ) and week 4 ( $P = 0.004$ ). Mean numerical rating scale pain scores were also significantly better in the group that received CMT. Adjusted mean back pain functional scale scores were significantly higher (improved) in the SMC plus CMT group than in the SMC group at both week 2 ( $P < 0.001$ ) and week 4 ( $P = 0.004$ ).

**Conclusion.** The results of this trial suggest that CMT in conjunction with SMC offers a significant advantage for decreasing pain and improving physical functioning when compared with only standard care, for men and women between 18 and 35 years of age with acute LBP.

**Key words:** low back pain, chiropractic manipulation, military medicine, physical functioning. **Spine 2013;38:627–634**

Low back pain (LBP) is exceedingly common, costly, and a significant cause of long-term sick leave and work loss.<sup>1–4</sup> Lifetime prevalence has been estimated to be as high as 84%, with a median cost per quality-adjusted life year of \$13,015.<sup>5,6</sup>

Manipulative therapy delivered by doctors of chiropractic is commonly used to treat patients with LBP. At least 7.5% of US adults seek care from chiropractors annually, representing approximately 190 million patient visits.<sup>7,8</sup>

The majority of systematic reviews find that chiropractic manipulative therapy (CMT) seems to reduce pain and disability at least moderately for many patients with LBP.<sup>9–16</sup> Thus, current evidence from randomized trials within controlled settings indicates CMT's potential effectiveness for LBP, but the appropriate role of CMT in treating LBP within the healthcare delivery system has not been delineated. Although more than 200 studies exist evaluating the effects of manipulative therapy for LBP, there are few studies focusing on high-velocity low-amplitude (HVLA) for patients with acute LBP delivered by chiropractors that include a standard medical care (SMC) intervention in both treatment groups, include diverse racial and ethnic populations, and focus on younger adults.<sup>17</sup> Thus, we know very little about the impact of CMT on diverse populations in real-world settings.

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The manuscript submitted does not contain information about medical device(s)/drug(s).

Samueli Institute grant funds were received to support this work. Some of this work was conducted in a facility constructed with support from Research Facilities Improvement Grant (C06 RR15433) from the National Center for Research Resources, National Institutes of Health.

No relevant financial activities outside the submitted work.

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The primary aim of this pragmatic, patient-centered comparative effectiveness study was to assess whether the addition of CMT to SMC reduces pain and increases physical functioning compared with only SMC for the treatment of acute LBP.

## MATERIALS AND METHODS

### Study Design and Setting

This was a prospective, 2-arm randomized controlled trial pilot study comparing CMT plus SMC with only SMC in US active-duty military personnel. The study took place from February 2008 to June 2009 at William Beaumont Army Medical Center (WBAMC), Fort Bliss, El Paso, TX. According to the 2010 Census report, the racial make-up of the area was approximately 72% white, 15% black, 2% Asian, 2% American Indian and Alaska Native, less than 1% Pacific Islander, 9% other races, and 18% Hispanic or Latino.<sup>18</sup>

### Participants

Eligibility criteria included male and female US active-duty military personnel between 18 and 35 years of age with acute LBP, defined as LBP of less than 4 weeks duration. Soldiers were excluded if they were relocating or leaving the post within 6 weeks from the day of the screening, had LBP for more than 4 weeks, were pregnant, or had a condition in which CMT was contraindicated.

### Interventions

#### Standard Medical Care

The study did not restrict access to SMC or prescribe a SMC delivery protocol. Thus, both groups had normal access to the SMC typically provided to patients with LBP at WBAMC. Standard care included any or all of the following: a focused history and physical examination, diagnostic imaging as indicated, education about self-management including maintaining activity levels as tolerated, pharmacological management with the use of analgesics and anti-inflammatory agents, and physical therapy and modalities such as heat/ice and referral to a pain clinic.

#### Chiropractic Manipulative Therapy

Participants in the group receiving CMT in addition to SMC were scheduled for up to 2 visits weekly with a doctor of chiropractic (DC) for a period of 4 weeks. The initial visit with the DC included a focused history and physical examination and diagnostic imaging as indicated. Treatments consisted of HVLA manipulation as the primary approach in all cases, with ancillary treatments at the doctor's discretion, including brief massage, the use of ice or heat in the lumbar area, stretching exercises, McKenzie exercises, advice on activities of daily living, postural/ergonomic advice; and mobilization. HVLA manipulation involves a single load or impulse "thrust" to body tissues. Patients were placed in a lateral recumbent or side-lying position with the superior or free hip and knee flexed and adducted across the midline. The chiropractor

stabilized the patient's free leg with his own leg while holding the patient's superior shoulder. The manipulative load was applied by using a pisiform contact on the patient's lumbar spine or sacroiliac joint while preventing motion of the patient through stabilizing holds on the shoulder and hip. The single impulse load, or thrust, was delivered by a quick, short controlled movement of the shoulder, arm, and hand combined with a slight body drop.

### Outcome Measures

The prespecified primary outcomes for this study were back-related pain and physical functioning at 4 weeks. Pain was measured using the numerical rating scale (NRS) and physical functioning was measured using the Roland-Morris Disability Questionnaire (RMQ) and the Back Pain Functional Scale.<sup>19</sup> The NRS asks participants to rate their level of pain during the past 24 hours on an ordinal 11-point scale (0 = no LBP; 10 = worst possible pain). The minimal clinically important difference is a change of 2.5 points.<sup>20</sup> The modified RMQ assesses LBP-related disability and the minimal clinically important difference is estimated at 2 to 3.5 points.<sup>21,22</sup>

Secondary outcomes included patient satisfaction and global improvement. Satisfaction was measured with an 11-point NRS, by asking "How satisfied are you with the overall results of your care?" Responses were anchored with 0 equal to "not at all satisfied" and 10 equal to "extremely satisfied." Patients also were asked to rate improvement on a 7-point Likert scale by rating "Compared with your first visit, your back pain is:" with responses in the range of 1, that indicates "completely gone" to 7, that indicates "much worse." Outcome assessments occurred at baseline, 2 weeks and 4 weeks.

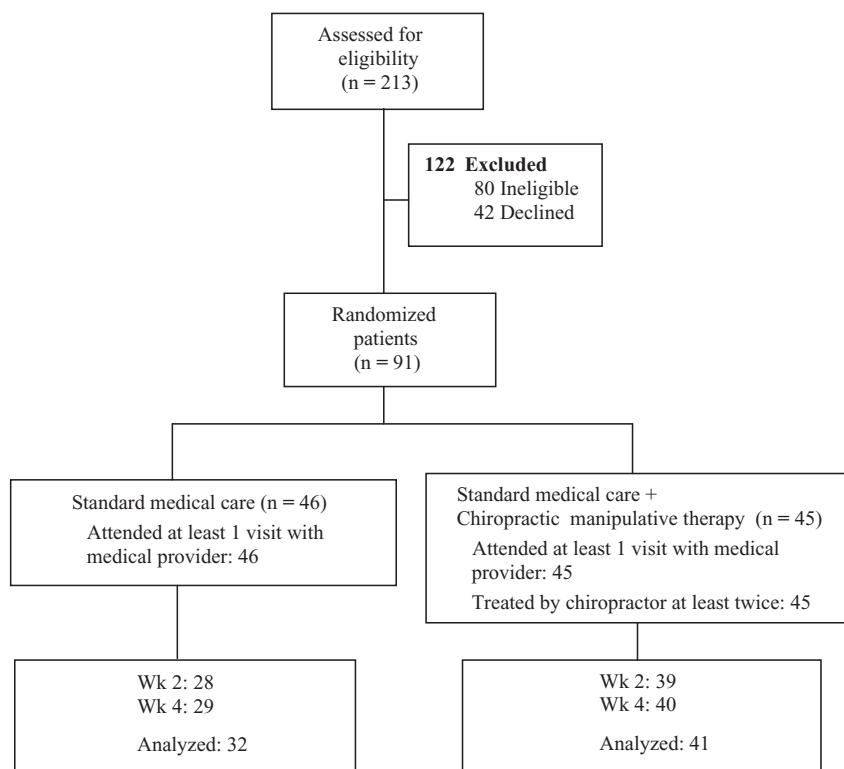
### Treatment Allocation

Randomization was achieved *via* a web-based minimization algorithm that balanced participant age, sex, and prescreen NRS between groups. Treatment allocation was conducted by the project manager through a web interface to the minimization algorithm. All future assignments were concealed. It was not possible to blind the participant or treating clinician to participant group assignment. However, the principal investigator and data analysts were blinded to treatment allocation.

### Statistical Methods

Our estimates of the standard deviations for RMQ and NRS were derived from several of our other trials of CMT for LBP. On the basis of this information, a sample size of 50 participants per group was determined for this pilot study. We estimated that this sample size would give us more than 80% power to detect group differences of 3 points on the RMQ. We had more than 70% power to detect differences of 1 point on the NRS and more than 90% to detect differences of 2 points.

Descriptive statistics were used to summarize participant characteristics at baseline for each treatment group. All analyses used an intention-to-treat approach. Linear mixed-effects models were fit for each of the 3 outcome variables over the week 2 and 4 endpoints. General covariance structures were



**Figure 1.** Flow diagram of participant screening, treatment allocation, and follow-up.

used in each model to account for within-participant correlation over time. Those who did not provide follow-up data at both 2 and 4 weeks were not included in the analyses. The models were adjusted for age, sex, prescreen NRS, and the baseline value of the respective outcome variable. Adjusted mean differences between the 2 treatment groups and 95% confidence intervals were reported for each final model.

## RESULTS

### Screening, Enrollment, and Follow-up

Participants were recruited from the Soldier and Family Medical Clinic at WBAMC and throughout Fort Bliss. The recruitment efforts included dissemination of flyers and posters at throughout the clinics, dining facilities, and Army Community Services. We also asked the medical providers for referrals of patients who met eligibility criteria. A total of 213 potential participants were screened for this study and 91 were enrolled (Figure 1). We extended the recruitment period by 3 months in attempt to meet our projected sample size of 100, but concluded recruitment at 91 participants when the grant period ended. Of those excluded, 80 did not meet eligibility criteria and 42 declined participation. A total of 46 participants were randomized to the SMC group and 45 were randomized to the SMC plus CMT group. Follow-up rates were 85% at both endpoints for the SMC plus CMT group and 61% and 63% for the SMC group at weeks 2 and 4, respectively.

### Baseline Characteristics

Study participants had a mean age of 26 years; 86% were male, and 63% were white. The median duration of

participant current LBP episode at the time of enrollment was 9 days and 43% had radicular signs. Most participants (71%) reported taking some medication for their back pain during the past week. Participants had a higher expectation of helpfulness for SMC plus CMT compared with only SMC (Tables 1 and 2).

### Study Treatments

The number of visits in the SMC group was in the range of 0 to 8, with a mean of 1.4 visits. The majority of participants (n = 24) in this group had only 1 visit. Medications were prescribed for 37% of the participants and included nonsteroidal anti-inflammatory drugs, muscle relaxants, benzodiazepines, analgesic creams, and narcotics. Thirty-three percent were placed on a treatment plan (exercise program, range of motion, stretching and modalities including heat and electrical stimulation) delivered primarily by a physical therapist. Fifty percent were given referrals, with a majority for physical therapy (38%) followed by radiographical evaluation (31%). The SMC group providers were physician assistants (28%), family practice physicians (18%), physical therapists (16%) or aides (12%), nurse practitioners (9%), or specialty providers (physical medicine [3%], athletic trainer [3%], and chiropractor [3%]).

Those assigned to SMC plus CMT had a mean of 1 visit for SMC (range, 0–4) and a median of 7 visits for CMT (range, 2–8). All patients received HVLA. In addition, patients may have received 1 or more of the following services provided by the DC: mobilization, brief massage, use of ice in the lumbar area, stretching exercises, McKenzie exercises, advice for activities of daily living, postural/ergonomic advice. Medi-

**TABLE 1. Descriptive Statistics of Demographic Variables at Baseline**

	Standard Medical Care (n = 46)		Standard Medical Care + CMT (n = 45)	
	n	%	n	%
Sex (male)	39	84.8	39	86.7
Age, mean (SD)	26.2	(4.8)	25.1	4.6
Race				
American Indian or Alaska Native	3	6.5	2	4.4
Asian	1	2.2	0	0.0
Native Hawaiian or other Pacific Islander	1	2.2	0	0.0
Black	10	21.7	10	22.2
White	24	52.2	33	73.3
Missing	7	15.2	0	0.0
Ethnicity				
Hispanic or Latino	8	17.4	7	15.6
Not Hispanic or Latino	35	76.1	37	82.2
Missing	3	6.5	1	2.2
Marital status				
Married or living with significant other	23	50.0	19	42.2
Divorced or separated	4	8.7	2	4.4
Never been married	12	26.1	23	51.1

CMT indicates chiropractic manipulative therapy; SD, standard deviation.

cations, including nonsteroidal anti-inflammatory drugs, muscle relaxants and narcotics, were prescribed to 18% of the participants in the SMC plus CMT group. Exercises, trigger point therapy, and modalities including heat and electrical stimulation were delivered by physical therapists to 6 participants.

### Pain and Functional Status

Mean RMQ scores decreased in both groups during the course of the study, but adjusted mean scores were significantly better in the SMC plus CMT group than in the SMC group at both week 2 ( $P < 0.001$ ) and week 4 ( $P = 0.004$ ) (Table 3). Mean NRS pain scores were also significantly better in the group that received CMT (Table 3). Adjusted mean Back Pain Functional Scale scores were significantly higher (improved) in the SMC plus CMT group than in the SMC group at both week 2 ( $P < 0.001$ ) and week 4 ( $P = 0.01$ ) (Table 3).

### Secondary Outcomes

Seventy-three percent of participants in the SMC plus CMT group rated their global improvement as pain completely gone, much better, or moderately better, compared with 17% in the SMC group (Figure 2). The mean satisfaction with care score on a 0 to 10 scale for the SMC plus CMT group was 8.9 at both weeks 2 and 4; the mean for the SMC group was 4.5 at week 2 and 5.4 at week 4 (Table 4).

Because of the disproportional loss to follow-up, we did a *post hoc* evaluation of the possible effects of this on the primary outcomes. We performed 15 imputations for missing values of the outcome variables from baseline demographic characteristics and pain and function scores. We combined the results to obtain estimates of regression coefficients, standard errors and  $P$  values and compared those with the results of the original analyses. The results of the multiple imputation analyses were similar to and consistent with the original analyses for all outcomes.

### Adverse Events

There were no serious adverse events (AEs). Two AEs graded as mild, expected events were reported by participants from the SMC plus CMT treatment arm. One AE was reported as sharp pain in the right buttocks that resolved within 24 hours; this AE was graded unrelated to trial interventions. The other AE was graded possibly related to the CMT when the participant reported sharp pain in the lower back that prompted a visit to the physician assistant for pain medication; this AE resolved within 48 hours.

### DISCUSSION

The results of our pragmatic pilot study indicate a statistically and clinically significant benefit to those receiving CMT in addition to SMC. Juni *et al*<sup>23</sup> conducted the only other study

**TABLE 2. Descriptive Statistics of Health Status Variables at Baseline**

	Standard Medical Care (n = 46)		Standard Medical Care + CMT (n = 45)	
	n	%	n	%
Duration of LBP episode (d)				
Mean (SD)	10.8	(8.7)	12.3	(8.3)
Median	7.0		11.0	
QTF diagnostic classification				
Pain without radiation	27	58.7	25	55.6
Pain + radiation to proximal extremity	10	21.7	14	31.1
Pain + radiation to distal extremity	9	19.6	6	13.3
BMI, mean (SD)	28.0	(3.9)	26.2	(4.3)
Current duty status				
Full duty	29	63.0	26	57.8
Profiled	17	37.0	19	42.2
Medications for back pain taken during past week				
Non-narcotic analgesics	23	50.0	21	46.7
NSAIDs	26	56.5	20	44.4
Sedatives/muscle relaxants	17	37.0	13	28.9
Narcotic analgesics	2	4.4	5	11.1
Antidepressants	1	2.2	4	8.9
Supplements	5	10.9	5	11.1
NRS (back pain during the past 24 hr; 0–10), mean (SD)	5.8	(2.1)	(5.8)	(1.5)
RMQ (0–24), mean (SD)	12.7	(5.1)	(11.0)	(4.2)
BPFS (0–60), mean (SD)	34.0	(11.2)	(34.0)	(8.4)
SF-12 Global Physical, mean SD	35.0	(8.9)	(36.6)	(6.4)
SF-12 Global Mental, mean (SD)	52.3	(10.9)	(49.5)	(9.3)

CMT indicates chiropractic manipulative therapy; NRS, numerical pain rating scale; RMQ, Roland-Morris Disability Questionnaire; BPFS, back pain functional scale; LBP, indicates low back pain; SD, standard deviation; BMI, body mass index; NSAID, nonsteroidal anti-inflammatory drug; SF-12, Short Form-12.

we found that compared only SMC with SMC plus CMT using the same outcome measures. They found no differences between the groups at 2 weeks using both the RMQ and NRS. CMT primarily included HVLA, whereas SMC consisted of medication and general home care advice. Participants underwent a single medical visit and 5 visits for CMT. Our study is similar to that conducted by Juni *et al*<sup>23</sup> with regard to the number of visits to DC and SMC, as well as the general treatment approaches provided within each group. However, there are differences in the populations studied. Our sample was younger and more ethnically diverse and included fewer women. Also, Juni *et al*<sup>23</sup> had substantially fewer losses to follow-up.

It is possible that our military population was also more physically fit at baseline than either the general population or previous study populations that evaluated CMT for LBP.

However, approximately 40% of our sample was profiled, meaning they had some duty restrictions due to their LBP. Although our sample may be, on average, more likely to be physically fit than young adults in general, when compared with a similar age cohort of the US population ages 25 to 34 using the Short Form-12 physical function scale, our population had a mean score of 36, whereas the norm is 53.<sup>24</sup> Therefore, our population had lower physical function than the general population at baseline because of their LBP. Mental function between our study population and the population norm were very similar (mean, 48 *vs.* 49 respectively).

Limitations to our study include an inability to blind both the participant and the treating clinician to treatment group assignment. However, both the principal investigator and analyst remained blinded throughout the study. Another limitation is a loss to follow-up that was disproportionate between



**TABLE 3. Adjusted Mean Differences for Standard Medical Care Versus Standard Medical Care Plus CMT on Primary Outcome Variables by Time Since Randomization**

	Adjusted Mean		Mean Difference*	95% CI*	<i>P</i>
	Standard Medical Care	Standard Medical Care + CMT			
RMQ (0–24)					
Week 2	12.9	8.9	3.9	1.8, 6.1	<0.001
Week 4	12.0	8.0	4.0	1.3, 6.7	0.004
NRS (0–10)					
Week 2	6.1	3.9	2.2	1.2, 3.1	<0.001
Week 4	5.2	3.9	1.2	0.2, 2.3	0.02
BPFS (0–60)					
Week 2	32.9	42.9	−10.0	−14.6, −5.5	<0.001
Week 4	35.3	43.0	−7.7	−12.9, −2.6	0.004

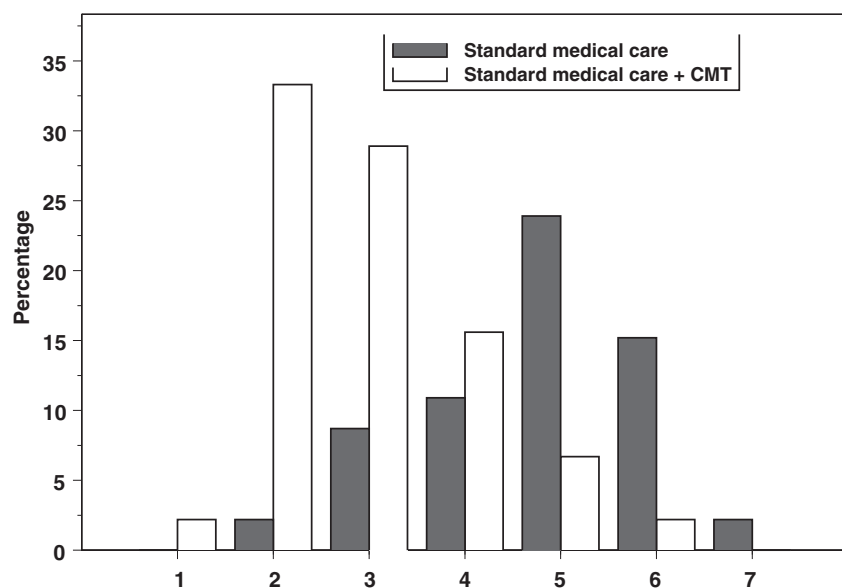
\*Estimated effects and 95% confidence intervals from linear mixed-effects models fitted with treatment group, visit (categorical), treatment group x visit interaction and general covariance structures and adjusted for age, sex, prescreen NRS, and baseline value of the respective outcome variable.

CMT indicates chiropractic manipulative therapy; NRS, numerical pain rating scale; RMQ, Roland-Morris Disability Questionnaire; BPFS, back pain functional scale.

groups. Although our loss to follow-up in the SMC plus CMT group was only 15%, we were unable to obtain follow-up assessments in more than 35% of the SMC group. This may have been because of the scheduling differences between the 2 groups. All CMT visits were scheduled at the first visit and coincided with the outcome assessments. However, follow-up visits in the SMC group were scheduled independently from treatment visits. Although the analyses of the imputed data did not differ from the analyses that included only the observed data, the possibility of attrition bias cannot be ruled out. Finally, while we tracked the prescription of medications at the outset of care, we did not gather detailed data regarding

actual medication use during the trial. Thus, it is possible that differences may have influenced study results. It is important to note that participants in the SMC group were twice as likely to have received medication as those in the SMC plus CMT group. It is difficult to attribute improvement to any 1 component of the care provided. Both treatment groups combined medication with physical modalities and medication was prescribed in less than half of the patients. However, our results suggest that the somewhat increased medication use in the SMC group did not confer a significant benefit.

This study answers some questions, while raising others. It will be important to attempt to replicate our findings using



**Figure 2.** Responses to Global Improvement Questionnaire administered at week-assessment visit. 1 indicates completely gone; 2, much better; 3, moderately better; 4, a little better; 5, about the same; 6, a little worse; 7, much worse. CMT indicates chiropractic manipulative therapy.

**TABLE 4. Participant Satisfaction With Care**

Assessment Visit	Standard Medical Care	Standard Medical Care + CMT
Satisfaction with overall results of care (0–10), week 2, mean (SD)	4.5 (2.9)	8.9 (1.2)
Satisfaction with overall results of care (0–10), week 4, mean (SD)	5.4 (2.9)	8.9 (1.5)

CMT indicates chiropractic manipulative therapy.

a larger sample size, with significant resources committed to follow-up strategies.

## CONCLUSION

The results of this trial suggest that CMT, in conjunction with SMC, offers a significant advantage for decreasing pain and improving physical functioning compared with only SMC, for active-duty men and women between 18 and 35 years of age with acute LBP when delivered in a pragmatic treatment setting. These findings are clinically significant and in contrast to Juni *et al.*<sup>23</sup> Differences could be largely because of the populations studied but may also reflect limitations in our study itself, including loss to follow-up. It is clear that additional high quality randomized controlled trials are required to establish the appropriate role definitively for CMT in diverse populations within pragmatic health care settings.

## ➤ Key Points

- Mean low back function scores improved in both groups during the course of the study but adjusted mean scores were significantly better in the group that received chiropractic manipulative therapy when compared with only SMC at both weeks 2 and 4.
- Adjusted pain scores were significantly improved in the group that received chiropractic manipulative therapy when compared with only SMC at both weeks 2 and 4.
- There was a statistically and clinically significant benefit to those patients receiving chiropractic manipulative therapy in addition to SMC for patients aged 18 to 35 years, with acute LBP.

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was approved for human subjects' research by the Institutional Review Boards of Palmer College of Chiropractic and William Beaumont Army Medical Center.

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